ESMRMB 2012
European Society for Magnetic Resonance in Medicine and Biology
29th Annual Scientific Meeting, October 4–6, Lisbon/PT

fDWI predicts obesity development in rats

e-Poster: 456

Congress: ESMRMB 2012

Type: Scientific Poster

Topic: Animal models – brain pathologies

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MeSH:

Hypothalamus [A08.186.211.577.482]

Obesity [C18.654.726.500]

Arcuate Nucleus [A08.186.211.730.385.357.352.081]

Ventromedial Hypothalamic Nucleus [A08.186.211.730.385.357.352.953]

Keywords: Obesity, Hypothalamic Nuclei, Functional Diffusion Weighted Imaging, Hypothalamic Activation

1. Purpose

Obesity is a pandemic syndrome underlying the most morbid and prevalent diseases in developed countries. It results from an imbalance in the appetite regulation, affecting global energy turnover. Our group has shown that appetite can be detected by MEMRI[1] and Diffusion Weighted Imaging (DWI) through changes in the hypothalamus of mice and humans[2, 3].

Here we show that changes observed by DWI are different in the hypothalamus of rats gaining weight or not under high fat diets, and that they affect differently the the Ventromedial Nucleus (VMN), the Arcuate Nucleus (ARC) and the Dorsomedeial Nucleus (DMN). Results suggest that global energy balance and response to diet can be monitored by DWI of the hypothalamus.

References [1]Delgado et al JCBFM (2011). [2]ESMRM 2011 (#103)[3], ISMRM 2012 (#3909)

2. Material and Methods

2.1 Animal model: Wistar rats (8 weeks, n=6) where fed ad libitum during 6 months with high-fat diet (17.4% Protein, 35.8%Lipids, 35% Carbohidrates, purified diet 230 HF, SAFE). Three rats developed obesity, weighting 638±11g ("Obese" group), and the remaining three showed a normal weigh 438±15g ("Non Obese" group).

2.2 DWI: Rats where anesthetized (1% isofluorane/oxygen) in a 7T magnet (90mm gradient coil-36G/cm, 23mm resonator) and imaged in a fed state and after an overnight fasting (δ=4ms, Δ=20ms, TR/TE=3000/51ms, in-plane resolution=0,296mm/pixel, axial slices 1.5mm, eight b-values $300<b<1800$ s/mm^2, L-R/A-P/H-F directions).

2.3 Data analysis: Data was analyzed in the Arcuate Nucleus (ARC), Ventromedial Nucleus (VMN) and Dorsomedial Nucleus (DMN). Signal decay with b values was compared between feeding conditions and fitted (MATLAB v7a) either to a

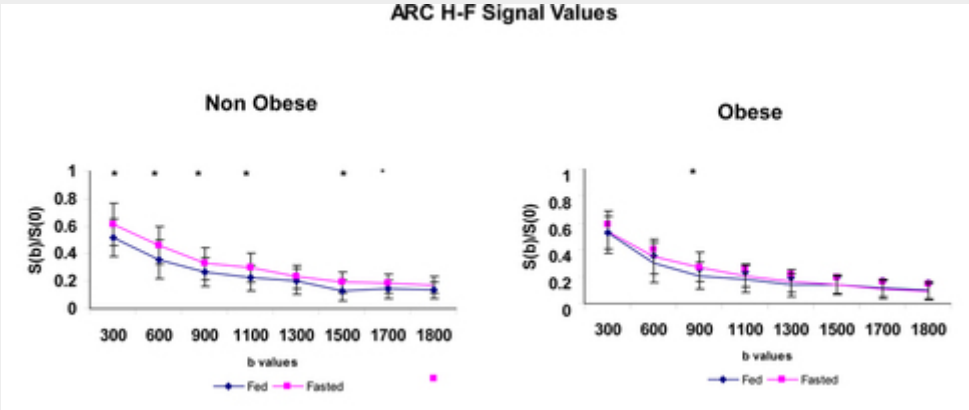
- monoexponential model, with $S(b)/S(0)=f\cdot\exp(-b\cdot ADC)$ for $300<b<600$ s/mm^2 or a
- biexponential model: $S(b)/S(0)=SDP\cdot\exp(-b\cdot D_{slow})+FDP\cdot\exp(-b\cdot D_{fast})$, with the slow (SDP) and fast (FDP) diffusion phases characterized by slow (D_{slow}) and fast (D_{fast}) diffusion coefficients, for the hole range of b values.

3. Results

3.1 Arcuate Nucleus

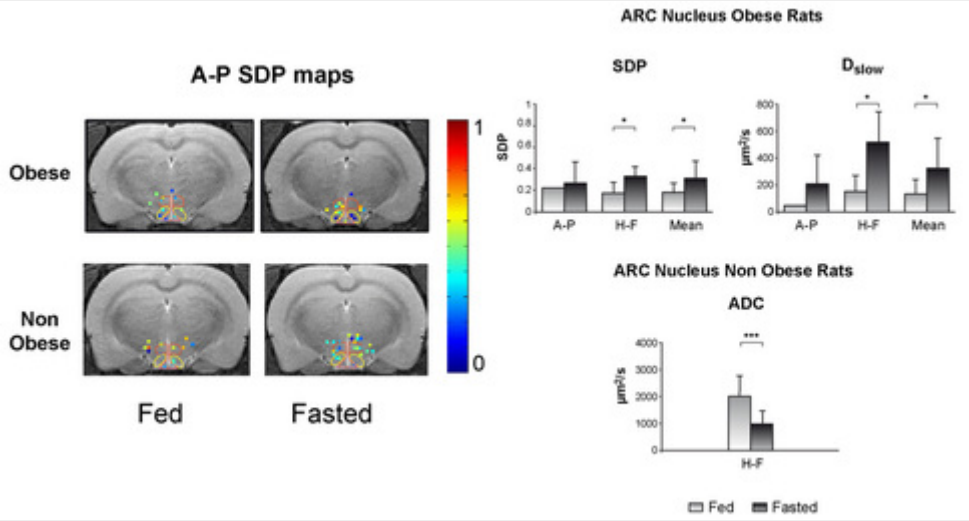
The signal decay of the H-F DWI in the area of the hypothalamic ARC for the fed and overnight fasted Obese and Non Obese Rats can be seen in figure 1.

Arcuate Nucleus H-F DWI signal decrease



Data was analyzed using monoexponential and biexponential models. Significant changes were found between fed and fasted Obese rats with biexponential comparisions, and between fed and fasted Non Obese Rats only with the monoexponential approach (Figure 2).

Figure 2. ARC activation in Obese and Non Obese Rats

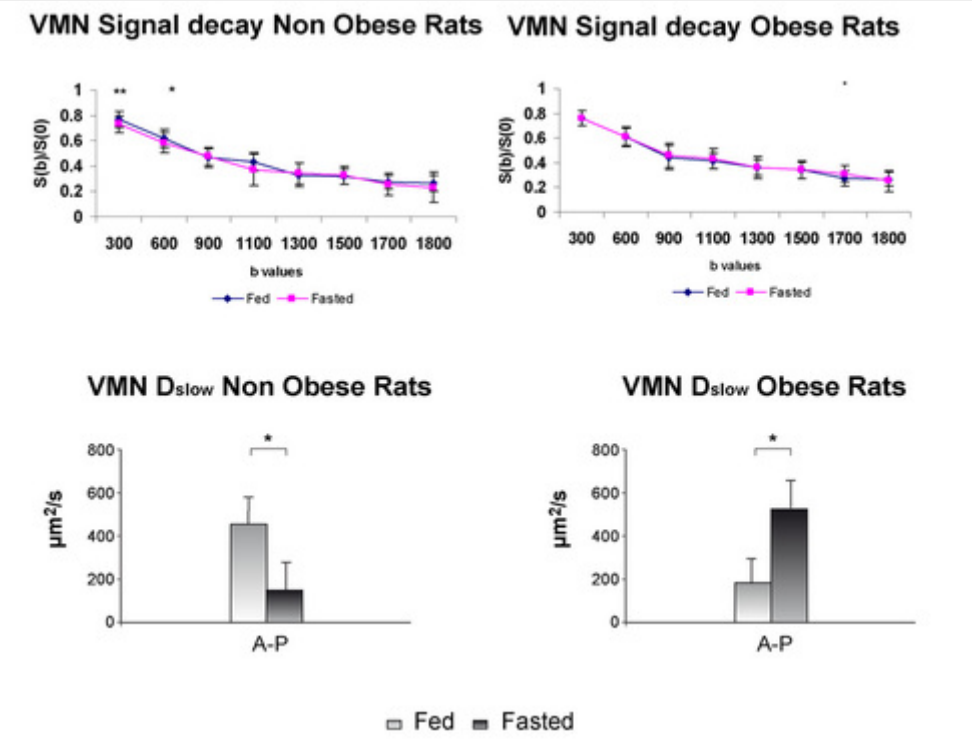


In figure 2, the main hypothalamic nuclei are shown superimposed to diffusion maps. DMN (red), VMN (yellow) and ARC (purpule).

3.2 Ventromedial Nucleus

The signal decay of the A-P DWI in the Ventromedial Nucleus for the fed and overnight fasted Obese and Non Obese Rats is shown in figure 3 (upper panels). SDP and D_{slow} values of the biexponential model showed significant differences between feeding conditions in the A-P direction (figure 3 bottom panels).

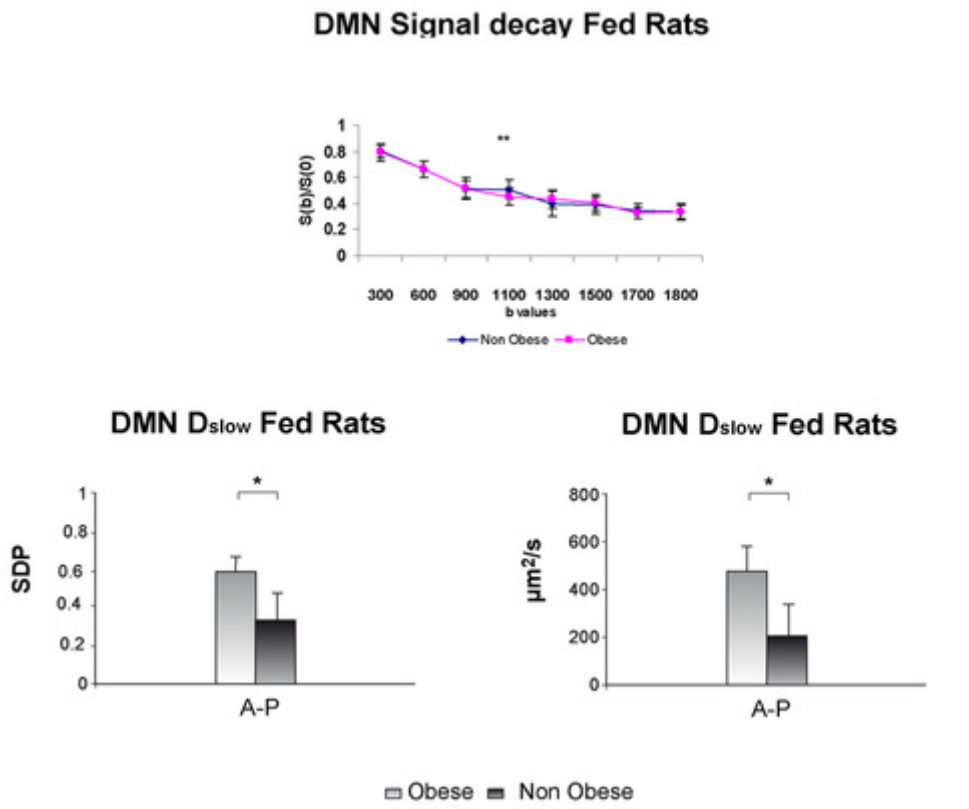
Figure 3. VMN activation with fasting in Obese and Non Obese Rats



3.3 Dorsomedial Nucleus

The signal decrease with the b values in the DMN of the Obese and Non Obese rats is depicted in figure 4 (upper panel), only for the fed state. In this feeding condition, Non Obese rats show increased SDP and D_{slow} (figure 4 lower panels).

Figure 4. DMN behavior in fed state in the Obese and Non Obese Rats



4. Conclusion

- Increments of SDP and D_{slow} are associated to **activation-induced astrocytic swelling**[2-4]. Here, we report significant **increments of SDP and D_{slow}** with fasting in the orexigenic **ARC** and **VMN** hypothalamic nuclei[1] in Obese rats (rats responding to HF diet). In the **fed** state, Non Obese Rats (rats not responding to HF diet) show **higher values** of **SDP and D_{slow}** in the **DMN,** in comparision to Obese Rats, indicating higher DMN activity.

- Differences obtained after the monoexponential fitting with low b values, idicate **increased ARC ADC** coefficients with fasting only in the **Obese Rats**, suggesting an **increased of flow** components not detecatble in Non Obese rats (rats not responding to HF diet).

- Our results suggest that obesity development may be identified through quantification of DWI parameters of hypothalamic nuclei.

References [1]Delgado et al JCBFM (2011). [2]ESMRM 2011 (#103)[3], ISMRM 2012 (#3909) [4]Le Bihan D et al. PNAS (2006)

5. Mediafiles

Arcuate Nucleus H-F DWI signal decrease

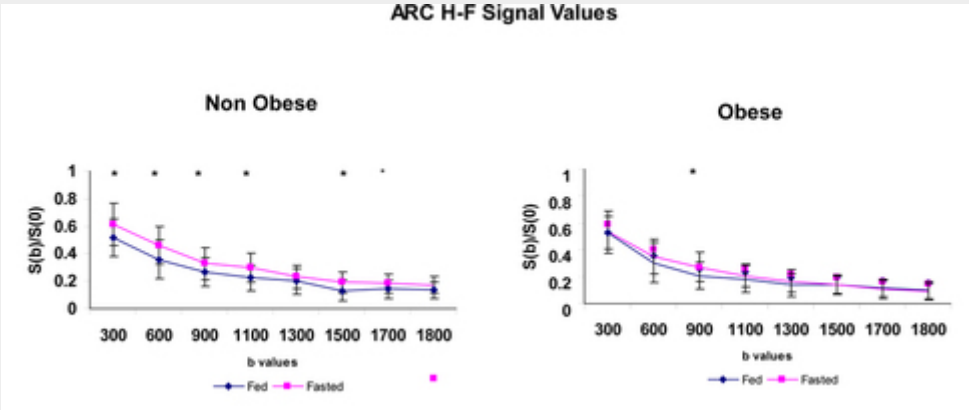


Figure 2. ARC activation in Obese and Non Obese Rats

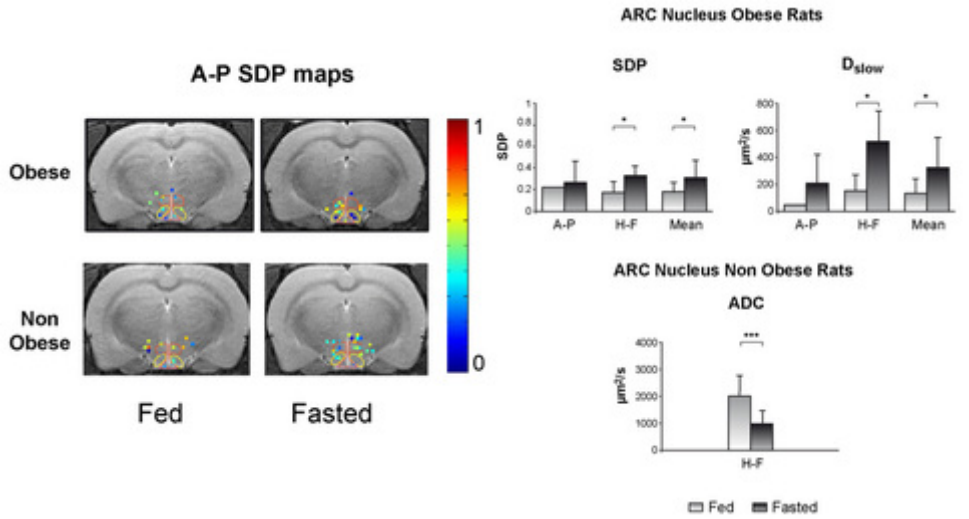


Figure 3. VMN activation with fasting in Obese and Non Obese Rats

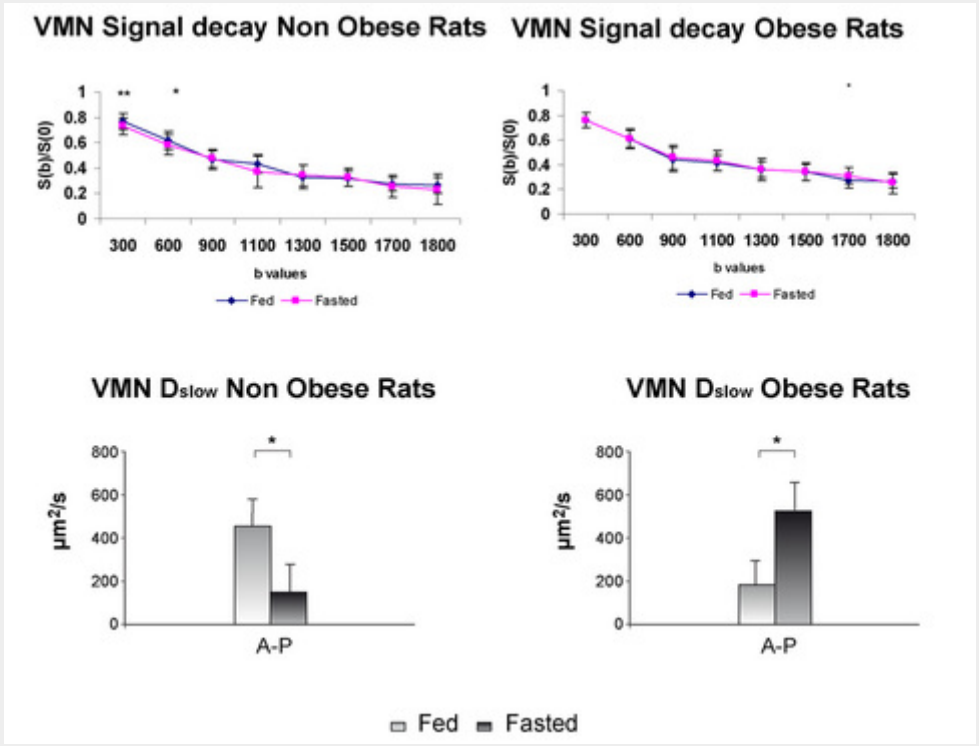


Figure 4. DMN behavior in fed state in the Obese and Non Obese Rats